

Amendments to the Drawings:

Figures 1, 4, and 5 have been deleted. Two replacement sheets of drawings are attached to this Amendment, each identified as "Replacement Sheet" in the top margin.

REMARKS

A. Status of the Claims

Claim 9 is amended to correct typographical errors. Thus, no new matter is added with this amendment. Therefore, claims 1, 9, 10, 11 and 14 are pending with entry of this amendment.

B. Objection to Drawing

The Examiner has objected to the drawings under 37 CFR 1.83(a). In response, Figures 1, 4, and 5 have been cancelled.

Applicants respectfully note that drawings are not required if not necessary for the understanding of the invention. See MPEP § 608.02(I). Moreover, where at least one process claim is present, a drawing is not required for a filing date under 35 U.S.C. §11 and 113. See MPEP § 608.02 (III). Applicants respectfully submit that the invention is clear as currently described in the pending application. Therefore, withdrawal of the rejection under 37 CFR 1.83(a) is requested.

C. Rejection Under 35 U.S.C. §112, Second Paragraph - Indefiniteness

The Examiner has rejected claim 9 for the recitation of "the sample." The term "sample" has been substituted with "droplets" to more clearly claim that which Applicants regard as their invention.

D. Rejection Under 35 U.S.C. §103(a)

Claims 1, 9 and 10 have been rejected as allegedly obvious over Bemish (U.S.P. 6,660,999). The Examiner asserts that Bemish discloses a proton source for producing a proton beam having an energy of 7.05 eV. The Examiner further asserts that it would have been obvious to modify the methods of Bemish by using electrospray ionization sources and heteroatom organic analytes disclosed in Kato (U.S.P. 6,541,767).

Applicants respectfully submit that a *prima facie* case of obviousness has not been established because:

- (1) Neither Bemish nor Kato teaches or suggests exposing analytes to a proton beam as recited in Applicants' claim 1;
- (2) Neither Bemish nor Kato teaches or suggests the use of a proton beam having an energy from 5 to 10 eV;
- (3) One skilled in the art would have no motivation to modify the methods of Bemish; and
- (4) One skilled in the art would have no reasonable expectation of successfully modifying the methods of Bemish to arrive at Applicants' claimed method.

1. Burden of Proof in Establishing Prima Facie Obviousness

"The examiner bears the burden of establishing a *prima facie* case of obviousness. *In re Rijckaert*, 9 F.3d 1531, 1532, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993); *In re Oetiker*, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992). Only if this burden is met does the burden of coming forward with rebuttal arguments or evidence shift to the applicant. *Rijckaert*, 9 F.3d at 1532, 28 USPQ2d at 1956. When the references cited by the examiner fail to establish a *prima facie* case of obviousness, the rejection is improper and will be overturned. *In re Fine*, 837 F.2d 1071, 1074, 5 USPQ2d 1596, 1598 (Fed. Cir. 1988)." See *In re Deuel*, 51 F.3d 1552, 34 USPQ2d 1210, 1214 (Fed. Cir. 1995).

In order to establish a *prima facie* case of obviousness, the rejection must demonstrate that (1) the cited references teach all the claimed elements; (2) there is a suggestion or motivation in the prior art to modify or combine the reference teachings; and (3) there is a reasonable expectation of success. MPEP § 2143; *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991). As explained below, Applicants submit that the cited references do not teach all of the claimed elements, do not provide a suggestion or motivation to modify the methods of the cited references, and fail to provide a basis for one of skill to reasonably expect that Applicants' methods would be useful in increasing the unbalanced charge of electrospray droplets.

The Federal Circuit has recently held that "[m]ost if not all inventions arise from a combination of old elements... Thus, every element of a claimed invention may often be found in

the prior art...However, identification in the prior art of each individual part claimed is insufficient to defeat patentability of the whole claimed invention...Rather, to establish obviousness based upon a combination of the elements disclosed in the prior art, there must be some motivation, suggestion or teaching of the desirability of making the specific combination that was made by the applicant." *See In Re Kotzab*, 217 F.3d 1365, 1369-1370 (Fed.Cir. 2000)(citations omitted)

In addition to suggesting or motivating one of ordinary skill in the art to combine the prior art to make the claimed invention, the prior art must also have taught that such a combination would have a "reasonable expectation of success." *In re Vaeck*, 947 F.2d 488, 493 (Fed.Cir. 1991). "'Obvious to try' has long been held not to constitute obviousness." *In re Deuel*, 51 F.3d 1552, 1559 (Fed.Cir. 1995). In addition, "[e]vidence showing there was no reasonable expectation of success may support a conclusions of nonobviousness." *See* MPEP § 2143.

2. Bemish and Kato Do Not Teach All of the Claimed Elements

Bemish discloses a method for mass spectrometry in which protons are added to helium droplets, in the *absence* of analyte, to form a protonated helium droplet. The analyte is then introduced to the protonated helium droplet after cooling to an appropriate temperature. The Bemish invention is clearly set forth in the Abstract, which states:

A method and device for mass spectrometry analysis, wherein a mass spectrometer is adapted for use with helium droplets, as an ionization site medium, *with a proton being initially captured by a large helium droplet* (~10,000 helium atoms) and then cooled evaporatively to 0.4 Kelvin. *The protonated helium droplet then picks up a neutral molecule* of interest and the neutral molecule is protonated inside of the droplet with the liquid helium droplet acting as a heat bath to provide rapid cooling of the newly formed protonated molecule (emphasis added).

See also Figure 1; Column 4, lines 54-66, and Column 5, lines 14-16. In contrast, Applicants' claim 1 explicitly recites that the analyte is exposed directly to a proton beam: "... *the electrospray droplets contain solvent and analytes; and exposing the electrospray droplets to a*

proton beam" Therefore, Bemish fails to teach or suggest the elements of claim 1 in which analytes are exposed to a proton beam.

Moreover, Bemish fails to teach or suggest a proton beam having an energy "from 5 to 10 eV" as recited in Applicants' claim 1. The Examiner points to Column 5, lines 31-38 for the proposition that Bemish's mention of "7.5 eV" discloses this element. However, the "7.5 eV" mentioned by Bemish does not refer to the energy of a proton beam. Rather, the "7.5 eV" is in reference to "the difference in proton affinity between helium and C₆₀." See Column 5, lines 34-35. In this passage, Bemish is discussing the energy difference in proton affinity between helium and C₆₀ in order to approximate the necessary number of helium atoms within a droplet to sufficiently cool C₆₀ to avoid C₆₀ fragmentation. See Column 5, lines 31-33, stating: "When the neutral molecule and the proton form a complex, the energy released results in helium boiling off the droplet."

Kato fails to remedy the deficiencies of Bemish. Therefore, Bemish and Kato fail to teach or suggest (1) exposing analytes to a proton beam as recited in Applicants' claim 1; and (2) teach or suggest the use of a proton beam having an energy from 5 to 10 eV.

Because Bemish and Kato fail to teach or suggest all the elements of claim 1, Applicants respectfully request withdrawal of the rejection.

3. One Skilled in the Art Would Have No Motivation to Modify the Methods of Bemish

Applicants respectfully submit that Bemish fails to provide a motivation to modify the disclosed methods to arrive at Applicants' claimed invention. There is no deficiency identified in Bemish that might motivate one skilled in the art to expose the analytes to a proton beam, or adjust the proton beam energy to a range of 5 to 10 eV. In fact, Bemish touts the advantages of the disclosed methods: "The method and device of the present invention offers several significant advantages over current analytical technology, namely by giving the percent composition (molar) without the need for standards and by obviating the need for chromatographic separation before mass analysis." See column 4, lines 14-19.

The only motivation to expose the analytes to a proton beam, or adjust the proton beam energy to a range of 5 to 10 eV, is provided in Applicants' specification. However, it is well-established that the exercise of hindsight reconstruction of the prior art is impermissible. See *W.L. Gore & Associates Inc. v. Garlock Inc.*, 220 USPQ 303, 313 (Fed. Cir. 1983) (stating, "[t]o imbue one of ordinary skill in the art with knowledge of the invention in suit...is to fall victim to the insidious effect of a hindsight syndrome wherein that which only the inventor taught is used against its teacher").

Because Bemish fails to provide a motivation to modify the disclosed methods to arrive at the presently claimed invention, Applicants respectfully request withdrawal of the rejection.

4. One Skilled in the Art Would Have No Reasonable Expectation of Successfully Modifying the Methods of Bemish to Arrive at Applicants' Claimed method

Based on the disclosure of Bemish and Kato, one skilled in the art would have no reasonable expectation of successfully modifying the methods of Bemish to arrive at Applicants' inventions. In fact, Bemish indicates that the size and temperature of the helium droplet should be carefully controlled at the time of contact with the analyte in order to avoid fragmentation of the analyte. See Column 3, lines 64-66; column 5, lines 14-60; and Abstract. One skilled in the art would reasonably expect that modifying the methods of Bemish by contacting the helium droplet before, or simultaneously with, a proton beam would effect both the temperature and size of the helium droplet. Therefore, there would be no reasonable expectation of successful modification.

Because the cited references fail to teach that modification of the disclosed methods would have a "reasonable expectation of success," Applicants respectfully request withdrawal of the rejection. See *In re Vaeck*, 947 F.2d 488, 493 (Fed.Cir. 1991).

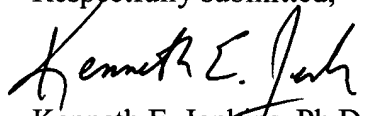
Appl. No. 10/696,549
Amdt. dated September 15, 2005
Reply to Office Action of August 3, 2005

PATENT

CONCLUSION

In light of the amendments and remarks detailed above, Applicants believe the claims are in condition for allowance. If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 858-350-6100.

Respectfully submitted,


Kenneth E. Jenkins, Ph.D.
Reg. No. 51,846

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, Eighth Floor
San Francisco, California 94111-3834
Tel: 858-350-6100
Fax: 415-576-0300
Attachments
KEJ:kej
60569295 v1